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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/532,033	08/09/2005	Jean-Pierre Vors	P/3610-57	6764

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EXAMINER	
ZAREK, PAUL E	

ART UNIT	PAPER NUMBER
1617	

MAIL DATE	DELIVERY MODE
07/29/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/532,033	VORS ET AL.	
	Examiner	Art Unit	
	Paul Zarek	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE _3_ MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 May 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-5,7-11,14-17,20 and 21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-5,7-11,14-17,20 and 21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 05/21/2009 has been entered.

Status of the Claims

2. Claims 3, 5, 7, 8, 11, and 16 have been amended, Claims 20 and 21 have been added, and Claims 6, 18, and 19 have been cancelled by the Applicant in correspondence filed on 04/16/2009. Claims 2-5, 7-11, 14-17, 20, and 21 are currently pending. This is the third Office Action on the merits of the claim(s).

RESPONSE TO ARGUMENTS

3. Claims 16, 2-5, 14, and 15 were rejected under 35 U.S.C. 102(b) as being anticipated by Charles, et al. (International Application No. WO 00/46184, already of record). Applicants traversed this rejection on the grounds that Charles, et al., does not anticipate treating *Candida albicans* or *Aspergillus fumigatus* in humans (to which the claim has been amended). Applicants contend that the disclosure of Charles, et al., that generically teaches the compounds, which are identical to those of the instant application, as being effective against Ascomycete spp. would be

expected to be effective *C. albicans* or *A. fumigatus*. Examiner respectfully disagrees. Charles, et al., discloses that the compounds disclosed therein would be effective to treat fungal infections of domestic or farm animals. It would be expected that such anti-fungal medication would also be effective for humans because it would be reasonably expected the herein claimed compounds to exhibit the same antifungal activity against the herein claimed pathogens regardless of the host, whether it is human or not. Moreover, Charles, et al., demonstrates that the compounds disclosed therein display broad spectrum anti-fungal activity. Indeed, the compounds disclosed therein are effective against *Erysiphe graminis, Pyricularia oryzae,* and *Leptosphaeria nodorum*, all of which belong to the phylum Ascomycota. The amendments to Claim 16 do not overcome this rejection. Therefore, the rejection of Claims 16, 2-5, 14, and 15 under 35 U.S.C. 102(b) as being anticipated by Charles, et al., is maintained.

4. Claims 16, 5-11, and 17-19 were rejected under 35 U.S.C. 103(a) as being unpatentable over Charles, et al., in view of Bennett (Goodman & Gillman, The Pharmaceutical Basis of Therapeutics, 10th ed., already of record). Applicants traversed this rejection on the grounds that Charles, et al., does not render obvious treating *C. albicans* or *A. fumigatus*. Examiner respectfully disagrees for the reasons discussed above. Applicants also traversed on the grounds that they demonstrate unexpected synergism with fluconazole and itraconazole. Applicants point to Table 6 as proof of the alleged unexpected synergism. Examiner respectfully disagrees. Applicants define the "level of interaction" (L.I.) between fluconazole/itraconazole with the claimed compounds as the ratio of the expected effected concentration to the observed concentration. An L.I. of greater than 1.5 is an indication of synergism, a L.I. of less than 0.5 is an indication of antagonism, and an L.I. between 0.5 and 1.0 is an indication of an additive

effect, which would be expected. Of the eight conditions disclosed in Table 6, three conditions demonstrate a synergistic effect, three conditions demonstrate an antagonistic effect, and two demonstrate an additive effect. Such a disclosure is not sufficient to prove drug synergy. The amendments to Claim 16 do not overcome this rejection. Therefore, the rejection of Claims 16, 5-11, and 17-19 were rejected under 35 U.S.C. 103(a) as being unpatentable over Charles, et al., in view of Bennett is maintained.

5. Newly added Claims 20 and 21 are examined below.

Claim Rejections - 35 USC § 103

6. The text of Title 35, U.S.C. § 102(b) can be found in a prior Office action.

7. Claims 20 and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Charles, et al. (above), in view of Bennett (above).

8. Newly added Claims 20 and 21 are drawn to the method of treating *C. albicans* or *A. fumigatus*, respectively, comprising the administration of a medicament comprising from between 0.5% and 99% of a combination of compound (I) (formula (I)) and compound (II) (additional antifungal compound).

9. Charles, et al., disclose an antifungal compound possessing the same number and identity of substituents claimed in the instant claims (pg 1, line 16 through pg 3, line 22). Compounds 364 and 365 (pg 46) correspond to N-ethyl-N-methyl-N'-[4-(4-chloro-3-trifluoromethylphenoxy)-2,5-dimethylphenyl]imidoformamide and N-ethyl-N-methyl-N'-[4-(4-fluoro-3-trifluoromethylphenoxy)-2,5-dimethylphenyl] imidoformamide, respectively, both of

which are claimed in Claim 17, from which Claims 20 and 21 depend (through Claims 11, 9, and 8). Charles, et al., contemplate treating fungal infestations in domestic and farm animals (pg 13, lines 32-33). Charles, et al., further teach that the compounds disclosed therein may be active against "general pathogens of . . . Ascomycete" (pg 10, lines 9-11). It is noted that both *C. albicans* and *A. fumigatus* belong to the phylum Ascomycota, and are thus considered Ascomycetes. Moreover, Charles, et al., demonstrates that the compounds disclosed therein display broad spectrum anti-fungal activity. Indeed, the compounds disclosed therein are effective against *Erysiphe graminis, Pyricularia oryzae,* and *Leptosphaeria nodorum*, all of which belong to the phylum Ascomycota. Charles, et al., do not teach a method of treating humans, combining compound I with another antifungal compound II, or having a synergistic effect with a second compound.

10. Both compound I and compound II are known to have antifungal effects (Charles, et al. [abstract], and Bennett [entire chapter], respectively). Bennett teaches that itraconazole can be used to treat candidiasis and aspergillosis (pg 1303-1304, "Therapeutic Uses"). Bennett also teaches that fluconazole can be used to treat candidiasis (pg 1305, "Therapeutic Uses. *Candidiasis*). Combining equivalents known for the same purpose is not a patentably distinguishing feature (MPEP §2173.05). "It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980). Optimizing the mass ratio of compounds I and II or adjusting the composition such that compounds I and II comprise 0.5-

99% of the medicament is also not a patentably distinguishing feature (MPEP § 2144.05 II). "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). It would be expected that such anti-fungal medication would also be effective for humans because it would be reasonably expected the herein claimed compounds to exhibit the same antifungal activity against the herein claimed pathogens regardless of the host, whether it is human or not. Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art to modify the teachings of Charles, et al., to incorporate the teachings of Bennett to for the method of treating *C. albicans* or *A. fumigatus* infestations in humans comprising formula (I) (compound I) and a second antifungal compound (compound II).

Conclusion

11. Claims 2-5, 7-11, 14-17, 20, and 21 are rejected.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Paul Zarek whose telephone number is (571) 270-5754. The examiner can normally be reached on Monday-Thursday, 7:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

PEZ

/San-ming Hui/
Primary Examiner, Art Unit 1617